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| 08/340,664 | 11/16/94 | GAUTVIK | K FORSK3.0001 |

EXAMINER
SPECTOR,L

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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 3/8/96 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

**Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:**

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

**Part II SUMMARY OF ACTION**

1. ☒ Claims 1, 6-10, 12, 14, 16-20, 21-28 are pending in the application.
   Of the above, claims remain are withdrawn from consideration.
2. ☒ Claims 6-10, 12, 14, 16-20 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☐ Claims _____ are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

**EXAMINER'S ACTION**

**Part III: Detailed Office Action**

Claim 2-5, 11, 13 and 15 have been cancelled. Claim 1 is amended. Claims 1 and 21-28 are under consideration.

The rejection of Claim 2 under 35 U.S.C. §112, first paragraph is moot in view of the cancellation of the claim.

The rejection of claim 3 under 35 U.S.C. , § 102(b) as being anticipated and of claims 1, 2, 4, 5, 11, 13 and 15 under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Kumagaye et al (J. Chrom. 327:327) or Kimura et al. (BBRC 114:493) or Fairwell et al. (Biochem. 22:2691) is withdrawn. Two declarations were submitted under 37 C.F.R. §1.132 in response to the above-withdrawn rejection.

The declarations submitted with the response of 3/8/96 have been fully considered to the following effect:

*The Maggio Declaration:*

The Maggio Declaration was *not* persuasive in overcoming the rejection over Kumagaye, Kimura or Fairwell. At paragraph 10, Dr. Maggio states that *Fairwell's* protocol was "rerun by *Kimura* et al. and the results, as illustrated in the chromatogram in Fig. 2 thereof, show significant impurities." This argument has been fully considered but is not deemed persuasive. First, the Examiner is not persuaded that the protocols of Fairwell and Kimura are identical or would produce identical results. For example, compare the first full paragraph of the second column, page 692 of Fairwell, with paragraphs 1 and 2 of page 494 in Kimura; it appears that Fairwell performed a more careful and detailed purification. As the methods of Fairwell and Kimura appear to differ, and as Kimura did not cite the Fairwell reference, the Examiner cannot accept the assertion that Fairwell's method was "rerun" by Kimura.

At Paragraphs 11 and 12, Dr. Maggio states that *Kimura* and *Kumagaye* did not produce an "essentially pure" hPTH. This argument has been fully considered but is not deemed persuasive, as the metes and bounds of "essentially pure" have not been set forth clearly in the specification. Therefore, the Examiner cannot accept the equation of "essentially pure" with "homogeneous". Despite the "shortcomings" of BOC synthesis of peptides as outlined at

paragraphs 13-16, it remains that the terminology of "essentially pure", in the absence of any clear definition to the contrary, cannot be construed to exclude such peptides.

The remainder of Dr. Maggio's declaration relates to and is duplicative of the declaration under 37 C.F.R. §1.132 by Dr. Gautvik. The Gautvik declaration is considered below.

*The Gautvik Declaration:*

The Gautvik declaration has been fully considered and is persuasive to establish that recombinantly produced hPTH possesses properties, namely increased maximal response as compared to synthetic hPTH, not possessed by synthetically produced hPTH. Thus, the rejection over Kumagaye, Kimura or Fairwell is withdrawn (see above). Although the arguments pertaining to purity on the basis of gels are not persuasive, due to inconsistent interpretation of smeared bands (which are stated to represent "overload" of the claimed peptide, but which are said to represent degradation of the synthetic peptide), as well as the presence of additional bands of high molecular weight with the *E. coli* preparation, which bands do not appear dissimilar to the high molecular weight bands of the Sigma preparation shown on Glossy "O", the establishment of different biological properties associated with the recombinantly made proteins is sufficient to overcome the art rejections over synthesized hPTH.

The Examiner does not agree with applicants' characterization of the interview which took place 2/21/96. The Examiner did not have, within the context of the interview, the time to critically evaluate the evidence proffered by applicants, but rather gave such a cursory review, and agreed that *if* the teachings therein were as characterized by the attorney, that such *might* be effective to overcome the rejections. It is for this reason that the interview summary, paper number 10, makes no reference to the withdrawal of any rejection. The removal of references by the proffered evidence has been accomplished in at least some instances, but is not the case for *all* of the cited prior art (see below).

***Formal Matters:***

Applicants are advised that numerous of the references cited in the information disclosure statement are no longer present in the parent files, and thus were unavailable to the Examiner. All considered references have been duly initialed. Any references listed on the PTO-1449 currently present in the case which were not considered but which applicants would like to have considered may be submitted with the response to this office action (and no later). Such references will be considered as part of the information disclosure statement submitted 8/31/95; thus, an additional PTO-1449 is unnecessary, and no fee or statement is required. The submission of any additional references must be made in accordance with the provisions of 37 C.F.R. §1.98.

The disclosure remains objected to because of the following informalities; Appropriate correction is required for each of the following items:

With respect to Figure 9, it is noted that while the description of the figure refers to panels A-E, only four panels are seen in the Figure, and only one of the four (B) is labelled. Correction is required.

Figure 10 is objected to because the quality of the submitted photocopy is poor. Applicants are required to substitute a "clean" copy of the Figure.

Figures 6 and 7, as submitted contained information placed too far to the top of the page, such that information was lost when holes were punched in the figures for insertion into the file wrapper by the Patent Office. Applicants should submit substitute copies of these figures, making sure that all information is sufficiently distant from the top of the page (allow at least one inch).

The Examiner notes applicants statement that these matters would be corrected at time of allowance. However, applicants are cautioned that the case cannot be processed for allowance until such matters have been corrected, therefore waiting until such time is impractical and could cause unnecessary delay.

The new title and other amendments to the specification are acknowledged and overcome the remaining objections to informalities.

***Double Patenting Rejections:***

Claims 1 and 21-28 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 6 of U.S. Patent No. 5,010,010. Although the conflicting claims are not identical, they are not patentably distinct from each other because although the protein claimed in the patent appears to be physically and functionally identical to the protein claimed in the pending claims, the instant claims are not restricted to protein which has been recombinantly produced in yeast cells. Although the patented claim is silent with respect to how pure the protein was, the protein is deemed to meet the purity limitations of the pending claims, alternatively it would have been obvious to purify the protein of the patented claim, using routine protein purification methodology, to be used for its known and expected properties.

Applicants intention to overcome this rejection by submission of a terminal disclaimer is noted.

***Objections and Rejections under 35 U.S.C. §112:***

Claims 1 and 21-28 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The metes and bounds of the newly introduced term "intact" are not clear. It is noted that the common usage of the term is to refer to something that is whole (e.g. not degraded), however alternative meanings include "not damaged in any way" (Webster's II New Riverside University Dictionary). It is not clear in what sense applicants intend the term, nor, if the latter definition is included, what constitutes "damaged". In the two declarations under 37 C.F.R. §1.132, it would appear that declarants are urging that the term excludes any *variant* of hPTH; however, such limitation cannot be imputed.

The metes and bounds of the newly introduced terms "substantially equivalent" and "essentially equivalent" are not clear. It cannot be determined whether the claimed proteins must have equivalent function to naturally occurring protein, or, if a range is implied, what that range would be. The Examiner notes that applicants have, at page 3 of the amendment, pointed to portions of the specification which provide literal support for the term "essentially", however no implicit support is seen at the other portions of the specification cited which would serve to indicate the intended meaning of the term.

With respect to claim 27, the metes and bounds of "fully active in an adenylate cyclase assay" are not clear; while a protein is described in the specification as being "fully active in an adenylate cyclase assay", the specification does not give any indication of what "full activity" is. Therefore, the metes and bounds of claims 27 and 28 are not clear.

***Rejections Over Prior Art:***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention

was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 1 and 21-28 are rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Brewer et al., U.S. Patent Number 3,886,132 for reasons cited in the previous Office Action, paper number 8 filed 9/8/95, at page(s)5-7.

The declaration by Dr. Maggio under 37 C.F.R. §1.132 is not persuasive to overcome this rejection. At paragraph 9, Dr. Maggio states that because Brewer et al. contains three errors in the amino acid sequence, that Brewer does not teach production of intact peptide. This argument has been fully considered but is not deemed persuasive because the protein purified by Brewer does indeed appear to have been intact, in the sense of not having been degraded or damaged. It cannot be concluded that a possible sequencing error indicates that the peptide was not "intact". The further argument of Brewer, pertaining to the purification of the synthesized 34 amino acid species is not relevant to the rejection, as Brewer was cited for the purification of naturally occurring hPTH, and not for the synthesis of the 34 amino acid fragment. Dr. Gautvik's declaration does not directly address this rejection.

Applicants argument that Brewer contains three incorrect amino acids in the disclosed sequence of the first 34 amino acids of the protein is not persuasive, both because the claims contain no limitation as to particular sequence, and because, even if Brewer sequenced the protein incorrectly, the protein itself, which was obtained from the natural source, appears to meet the limitations of the claims. The additional arguments pertaining to Brewer are drawn to the *synthetic* peptide of Brewer, and do not address the purified (naturally occurring) protein disclosed by Brewer, upon which this rejection is based.

***Advisory Information:***

No claim is allowed.

Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector, whose telephone number is (703) 308-1793. Dr. Spector can normally be reached Monday through Friday, 8:00 A.M. to 4:30 P.M.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ms. Garnette D. Draper, can be reached at (703)308-4232.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 308-0196.

Certain papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Group 1800 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The Art Unit 1812 Fax Center number is (703) 308-0294. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office. **Please** advise the Examiner at the telephone number above when a fax is being transmitted.

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5/21/96

GARNETTE D. DRAPER
SUPERVISORY PRIMARY EXAMINER
GROUP 1800